PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOD EURTUER							
X-16660	FOR FURTHER ACTION	as well	see Form PCT/ISA/220 as, where applicable, item 5 below.					
International application No.	International filing date (day/month	(vear)	(Earliest) Priority Date (day/month/year)					
memational application No.	and in the state of the state o	, , cur <i>)</i>	(Lamost, Fronty Date (day/month/year)					
PCT/US2005/006723 02/03/2005 15/03/2004								
Applicant								
ELI LILLY AND COMPANY								
This International Search Report has been according to Article 18. A copy is being tra			ority and is transmitted to the applicant					
This later and so all Control Boards are sinter	of a hadal of 17 also	-4-						
This International Search Report consists								
X It is also accompanied by	a copy of each prior art document ci	ted in this	report.					
A. David Albanian								
	international search was carried out less otherwise indicated under this it		is of the international application in the					
The international this Authority (Ru		of a transla	ation of the international application furnished to					
b. With regard to any nucle	otide and/or amino acid sequence	disclosed	in the international application, see Box No. 1.					
2. Certain claims were fou	nd unsearchable (See Box II).							
3. Unity of invention is lac	king (see Box III).							
4. With regard to the title,								
X the text is approved as su	ibmitted by the applicant.							
	shed by this Authority to read as follo	ws:						
	,,,							
}								
5. With regard to the abstract,								
X the text is approved as su	ubmitted by the applicant.							
l 😕 🗀		is Authorit	ty as it appears in Box No. IV. The applicant					
			ch report, submit comments to this Authority.					
6. With regard to the drawings ,								
a. the figure of the drawings to be p	published with the abstract is Figure	No						
as suggested by	the applicant.							
	is Authority, because the applicant fa	iled to suc	igest a figure.					
	is Authority, because this figure bette	_						
	-	, characte	migo die myembon.					
b none of the figures is to b	e published with the abstract.							

International Application No PCT/US2005/006723

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07C217/56 C07C C07C317/32 C07C233/25 C07C217/90 C07C233/73 C07C235/18 C07C323/41 C07D213/82 C07D307/68 C07D295/20 C07D261/18 C07D333/38 C07D231/14 C07D285/06 C07D241/44 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) CO7C CO7D IPC 7 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) EPO-Internal, PAJ, CHEM ABS Data, WPI Data, BEILSTEIN Data, BIOSIS, EMBASE C. DOCUMENTS CONSIDERED TO BE RELEVANT Category Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. √WO 03/002519 A (BAYER AKTIENGESELLSCHAFT; Χ 1,2,4,6, SCHMECK, CARSTEN; MUELLER, ULRICH; 7,11-15, SCHMIDT,) 9 January 2003 (2003-01-09) 17 page 33; claim 1 √FR 2 291 743 A (ROUSSEL UCLAFF) 1,2,4, X 18 June 1976 (1976-06-18) 6-9. 11 - 15, 17the whole document χ WO 02/12224 A (ORTHO MCNEIL 1-9. 11-15,17 PHARMACEUTICAL, INC) 14 February 2002 (2002-02-14) examples 6-9 claims 1,23 Patent family members are listed in annex. Further documents are listed in the continuation of box C. X Special categories of cited documents later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the "A" document defining the general state of the art which is not considered to be of particular relevance invention "E" earlier document but published on or after the international "X" document of particular relevance, the claimed invention filing date cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the "O" document referring to an oral disclosure, use, exhibition or document is combined with one or more other such doci ments, such combination being obvious to a person skilled in the art. other means "P" document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of mailing of the international search report Date of the actual completion of the international search 22/08/2005 1 August 2005 Name and mailing address of the ISA Authorized officer European Patent Office, P B 5818 Patentiaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx 31 651 epo nl, Steendijk, M Fax (+31-70) 340-3016

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International Application No
PCT/US2005/006723

C /Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	FC1/032005/006/23
Category °		Relevant to claim No.
X	PATENT ABSTRACTS OF JAPAN vol. 2000, no. 20, 10 July 2001 (2001-07-10) -& JP 2001 064176 A (SUMITOMO PHARMACEUT CO LTD; SUMITOMO CHEM CO LTD), 13 March 2001 (2001-03-13) abstract	1,2,4, 6-9, 11-15,17
X	✓WO 00/59878 A (ICOS CORPORATION; FOWLER, KERRY; ORME, MARK; STAUNTON, DONALD, E; ADOL) 12 October 2000 (2000-10-12) claims 1,7	1-9,11
X	VEP 1 113 000 A (AJINOMOTO CO., INC) 4 July 2001 (2001-07-04) claim 1; examples	1,2,4, 6-9,11
X	FP 1 193 255 A (AJINOMOTO CO., INC) 3 April 2002 (2002-04-03) claim 1; examples	1-3,5-9, 11
X	√US 5 084 449 A (SEYDEL ET AL) 28 January 1992 (1992-01-28) claims	1,2,4, 6-9,11
X	ÚS 3 976 784 A (COLES ET AL) 24 August 1976 (1976-08-24) claims	1,2,4, 6-9,11
X	✓US 2 456 258 A (DOHRN MAX ET AL) 14 December 1948 (1948-12-14) claims	1-3,5-9, 11
X	WENNER, WILHELM: "4-Aminomethyl-4'-aminodiphenyl sulfone and related compounds" JOURNAL OF ORGANIC CHEMISTRY, 22, 1508 -13 CODEN: JOCEAH; ISSN: 0022-3263, 1957, XP002338658 page 1512; table III	1,2,4, 6-9,11
X	SURREY, A. R. ET AL: "Sulfides and sulfones of pyridine and quinoline" JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, 62, 173 -4 CODEN: JACSAT; ISSN: 0002-7863, 1940, XP002338659 table 1	1-3,5-9, 11
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International Application No
PCT/US2005/006723

C.(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	PC1/US2005/006/23
Category °		Relevant to claim No.
X	US 5 883 096 A (LOWE ET AL) 16 March 1999 (1999-03-16) claim 1; example 747	1-9,11
X	EP 0 407 346 A (CIBA-GEIGY AG) 9 January 1991 (1991-01-09) page 15	1-3,5-9
X	DATABASE CAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; 1951, TAKAHASHI ET AL.: "Pyridine derivatives containing sulfur IV. Synthesis of nitro- and aminopyridines" XP002338663 retrieved from STN Database accession no. 1951:26999 abstract & YAKUGAKU ZASSHI , 62, 488-91 CODEN: YKKZAJ; ISSN: 0031-6903, 1942,	1-3,5-9
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A	/WO 99/33806 A (ORTHO-MCNEIL PHARMACEUTICAL, INC; CARSON, JOHN, R; CARMOSIN, RICHARD,) 8 July 1999 (1999-07-08) claim 1	1-17
P , X	WO 2004/093800 A (THE REGENTS OF THE UNIVERSITY OF CALIFORNIA; OREGON HEALTH & SCIENCE U) 4 November 2004 (2004-11-04) pages 8,45; claim 1	1,2,4, 6-9, 11-15,17
P,X	WO 2004/026305 A (ELI LILLY AND COMPANY; BLANCO-PILLADO, MARIA-JESUS; CHAPPELL, MARK, DO) 1 April 2004 (2004-04-01) page 232; example 381d	1-17

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Information on patent family members

International Application No
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				EP	0407346		09-01-1991
				JP	3044372		26-02-1991
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WO	9933806	Α	08-07-1999	AU	2009799		19-07-1999
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From the

PATENT COOPERATION TREATY

INTERNATIONAL SEARCHING AUTHORITY To: WRITTEN OPINION OF THE see form PCT/ISA/220 INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1) DEC 2005/ Date of mailing X 16660 (day/month/year) see form PCT/ISA/210 (second sheet) Applicant's or agent's file reference FOR FURTHER ACTION see form PCT/ISA/220 See paragraph 2 below International application No International filing date (day/month/year) Priority date (day/month/year) PCT/US2005/006723 02.03.2005 15.03.2004 International Patent Classification (IPC) or both national classification and IPC C07C217/56, C07C317/32, C07C233/25, C07C217/90, C07C233/73, C07C235/18, C07C323/41, C07D213/82, Applicant **ELI LILLY AND COMPANY** 1. This opinion contains indications relating to the following items: Box No. I Basis of the opinion ☐ Box No. II Priority Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability ☐ Box No. IV Lack of unity of invention ☑ Box No V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement ☑ Box No VI Certain documents cited ☐ Box No. VII Certain defects in the international application Box No. VIII Certain observations on the international application 2. **FURTHER ACTION** If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1 bis(b) that written opinions of this International Searching Authority will not be so considered. If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. For further options, see Form PCT/ISA/220. 3. For further details, see notes to Form PCT/ISA/220. Name and mailing address of the ISA Authorized Officer

Authorized Office



European Patent Office D-80298 Munich Tel +49 89 2399 - 0 Tx⁻ 523656 epmu d Fax +49 89 2399 - 4465

Steendijk, M

Telephone No +49 89 2399-8460



WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2005/006723

	Box N	o. I Basis of the opinion					
1.	With regard to the language , this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.						
	lai	nis opinion has been established on the basis of a translation from the original language into the following inguage—, which is the language of a translation furnished for the purposes of international search inder Rules 12.3 and 23.1(b)).					
2.	. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:						
	a. type	of material:					
		a sequence listing					
		table(s) related to the sequence listing					
	b. form	nat of material:					
		in written format					
		in computer readable form					
	c. time	of filing/furnishing:					
		contained in the international application as filed.					
		filed together with the international application in computer readable form.					
		furnished subsequently to this Authority for the purposes of search.					
3.	ha cc	addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto as been filed or furnished, the required statements that the information in the subsequent or additional pies is identical to that in the application as filed or does not go beyond the application as filed, as propriate, were furnished.					
4.	Addıtic	nal comments:					

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No. PCT/US2005/006723

	x No. III Non-establishment opticability	of op	inion with regard to novelty, inventive step and industrial				
			ntion appears to be novel, to involve an inventive step (to be non have not been examined in respect of:				
	the entire international applicat	tion,					
\boxtimes	claims Nos. 12-16						
be	cause:						
☒	the said international application, or the said claims Nos. 12-16 relate to the following subject matter which does not require an international preliminary examination (specify):						
	see separate sheet						
	the description, claims or drawings (indicate particular elements below) or said claims Nos. are so unclear that no meaningful opinion could be formed (specify):						
	the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.						
	no international search report has been established for the whole application or for said claims Nos.						
	the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:						
	the written form		has not been furnished				
			does not comply with the standard				
	the computer readable form		has not been furnished				
			does not comply with the standard				
	the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.						
	See separate sheet for further	detai	ils				

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims

10,16

No:

Claims

1-9,11-15,17

Inventive step (IS)

Yes: Claims No:

10,16 1-9,11-15,17

Industrial applicability (IA)

Yes: Claims

Claims

1-11,17

No: Claims

Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis 1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

- 1) The present application relates to diaryl ethers and analogues thereof useful as opioid antagonists (see table 1, pages 25-26).
- 2) The following documents are cited:

D1: WO 03/002519 A

D2: FR-A-2 291 743

D3: WO 02/12224 A

D4: JP 2001 064176 A

D5: WO 00/59878 A

D6: EP-A-1 113 000

D7: EP-A-1 193 255

DO 110 1 5 004 440

D8: US-A-5 084 449

D9: US-A-3 976 784

D10: US-A-2 456 258

D11: J.ORG.CHEM., 22, 1508 -13

D12: J.AM.CHEM.SOC., 62, 173 -4

D13: JP 2001 089412 A

D14: US-A-5 883 096

D15: EP-A-0 407 346

D16: CAPLUS [Online] accession no. 1951:26999

D17: CAPLUS [Online] accession no. 1963:14812

D18: WO 99/33806 A

D19: WO 2004/093800 A

D20: WO 2004/026305 A

Documents D19 and D20 were published after the priority claimed for the present application; on the presumption that the priority is validly claimed, these documents are not considered as prior art.

3) Search limitation

The initial phase of the search revealed such a great amount of documents relevant to the novelty of claims 1,2,4,6-9 and 11, that only a limited number of representative documents has been cited.

4) Novelty

The subject-matter of claims 1-9, 10-15 and 17 is considered anticipated by documents D1-D17 as cited in the search report.

In this context it is noted that the therapeutical indications of claims 12-15 and 17 are so broad, that the various indications mentioned in for instance D1-D4 may be considered as anticipating.

5) Inventive step

In as far as the claimed subject-matter is novel, i.e. relates to truly new compounds (e.g. claim 10) or truly new indications (e.g. claim 16) the claimed subject-matter may be considered to involve an inventive step.

Closest prior art seems D18 describing similar activity for biarylamino piperidines. It could not be foreseen that the present compounds provide for alternative agents with respect to D18.

6) Further observations

Claims 12-16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Claim 5 is unclear in its formulation as it actually seems to comprise the features of two different claims.